Abstract

The present invention provides a method of inhibiting the development of opioid tolerance using novel chimeric hybrid molecules ~~containing an opioid moiety of chemically modified morphine (3) that binds to and activates the human mu-(μ) opioid receptor, with the opioid moiety linked through a novel linker hinge (4) to a substance P peptide fragment moiety (5) that binds to and activates the human substance P receptor. The hybrid alkaloid/peptide analgesics may be administered intrathecally, systemically or orally~~ by administering to a living subject a conjugate molecule of a general class of chimeric hybrid conjugate molecules capable of simultaneous activation of MOR and SPR receptors within the CNS and of engendering efficacious opioid-dependent analgesia over a time course of administration without loss of analgesic potency.